

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method to enhance bone formation or to treat pathological dental conditions or to treat degenerative joint conditions in a vertebrate animal, which method comprises administering to a vertebrate subject in need of such treatment an effective amount of a compound ~~that inhibits the activity of NF- κ B or~~ that inhibits proteasomal activity or that inhibits production of proteasome proteins wherein the compound does not inhibit the isoprenoid pathway.

2. (Canceled)

3. (Currently amended) The method of claim 1[[2]], wherein the compound inhibits the chymotrypsin-like activity of the proteasome.

4. (Original) The method of claim 3, wherein the compound is a peptide having at least 3 amino acids and a C-terminal functional group that reacts with the threonine residue of the chymotrypsin-like catalytic site of the proteasome.

5. (Original) The method of claim 4, wherein the c-terminal functional group is selected from the group consisting of an epoxide, a -B(OR)₂ group, a -S(OR)₂ group and a -SOOR group, wherein R is H, an alkyl (C₁₋₆) or an aryl (C₁₋₆).

6. (Original) The method of claim 5, wherein the functional group is an epoxide that forms a morpholino ring with the threonine residue of the chymotrypsin-like catalytic site of the proteasome.

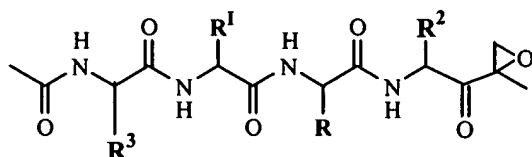
7. (Original) The method of claim 3, wherein the peptide is a peptide α' , β' -epoxyketone.

8. (Original) The method of claim 7, wherein the peptide α' , β' -epoxyketone has at least 4 amino acids.

9. (Original) The method of claim 7, wherein the c-terminus amino acid of the peptide α', β' -epoxyketone is a hydrophobic amino acid.

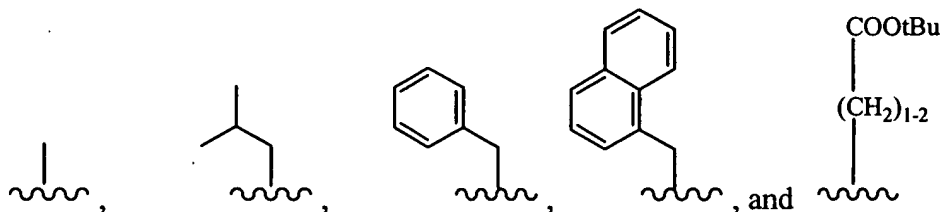
10. (Original) The method of claim 9, wherein the hydrophobic amino acid is leucine or phenylalanine.

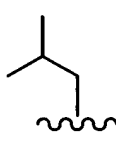
11. (Currently Amended) The method of claim 7, wherein the peptide α', β' -epoxyketone has the following formula:

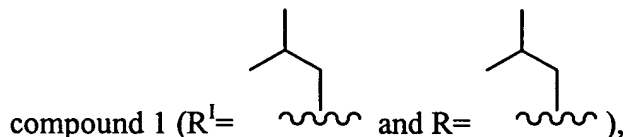


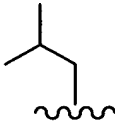

wherein each of R, R¹, R² and R³ is a ~~hydrophobic~~ hydrophobic substituent.

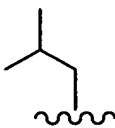
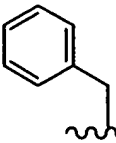
12. (Original) The method of claim 11 wherein each of R, R¹, R² and R³ is independently selected from the group consisting of

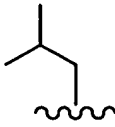
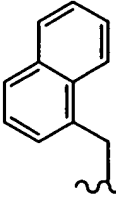



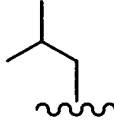
13. (Original) The method of claim 11, wherein R² and R³ are  and the compound is selected from the group consisting of

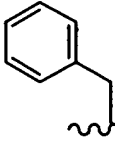
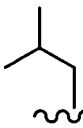


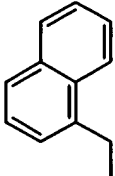
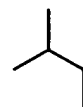
compound 2 ($R^1 =$  and $R =$ ) ,

compound 3 ($R^1 =$  and $R =$ ) ,

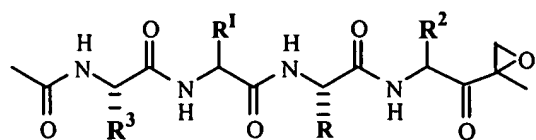
compound 4 ($R^1 =$  and $R =$ ) ,

compound 5 ($R^1 =$  and $R =$ ) ,

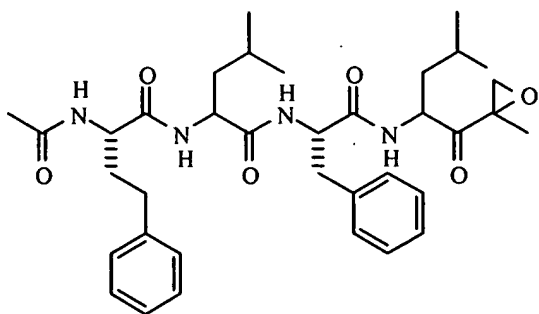
compound 6 ($R^1 =$  and $R =$ ) and

compound 7 ($R^1 =$  and $R =$ ) .

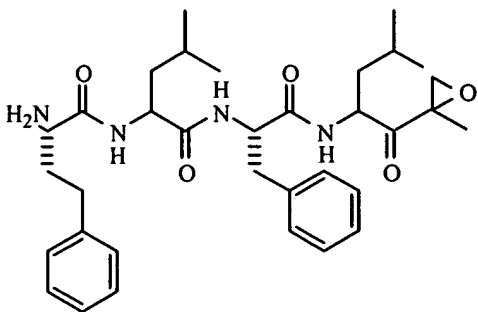
14. (Original) The method of claim 11, wherein the peptide α' , β' -epoxyketone has the following stereo-configuration:



17. (Original) The method of claim 16, wherein the peptide α' , β' -epoxyketone is

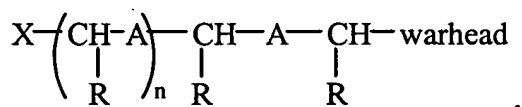


18. (Currently Amended) The method of claim 3, wherein the compound is selected from the group consisting of



, epoxomicin, pyrazylcarbonyl-Phe-Leu-Boronate (PS-341), tri-leucine vinyl sulfone (NLVS), N-carbobenzoyl-Ile-Glu-(OtBu)-Ala-Leu-CHO (PSI) epoxide, lactacystin, ~~pentoxifylline (PTX)~~ and a peptidyl aldehyde.

19. (Original) The method of claim 3, wherein the compound has the following formula:



wherein the warhead reacts irreversibly with the catalytic chymotrypsin site of the proteasome;

A is independently CO-NH or isostereomer thereof;

R is independently a hydrocarbyl;

X is a polar group; and

n = 0-2.

20. (Original) The method of claim 19, wherein R contains a substituted group selected from the group consisting of a halo group, -OR, -SR, -NR₂, =O, -COR, -OCOR, -NHCOR, -NO₂, -CN, and -CF₃.

21. (Original) The method of claim 19, wherein X is protected.

22. (Original) The method of claim 1, wherein the subject is characterized by a condition selected from the group consisting of osteoporosis, bone fracture or deficiency, primary or secondary hyperparathyroidism, periodontal disease or defect, metastatic bone disease, osteolytic bone disease, post-plastic surgery, post-prosthetic joint surgery, and post-dental implantation.

23. (Original) The method of claim 1, which further comprises administering to the subject one or more agents that promote bone growth or that inhibit bone resorption.

24. (Original) The method of claim 23, wherein the agents are selected from the group consisting of bone morphogenetic factors, anti-resorptive agents, osteogenic factors, cartilage-derived morphogenetic proteins, growth hormones, estrogens, bisphosphonates, statins and differentiating factors.

25-43 (Canceled)